941,664

PATENT SPECIFICATION

NO DRAWINGS

941,664

Date of Application and filing Complete Specification Feb. 19, 1960.

No. 5921/60.

Application made in United States of America (No. 794753) on Feb. 19, 1959.

Complete Specification Published Nov. 13, 1963.

© Crown Copyright 1963.

Index at acceptance:—A5 B2Z.

International Classification:—A61k

COMPLETE SPECIFICATION

Buccal or Sublingual Tablet containing Carbohydrase Enzyme for Controlling Inflammation

We, HENRY THOMPSON STANTON, Jr., JAMES HARRISON STANTON, CHARLES COLLIER STANTON and O'NEILL RYAN, Jr., all Citizens of the United States of America, trading as the firm RYSTAN COMPANY, of 7,

SPECIFICATION NO. 941,664

By a direction given under Section 17 (1) of the Patents Act 1949 this application proceeded in the names of HENRY THOMPSON STANTON, JUN., JAMES HARRISON STANTON and CHARLES COLLIER STANTON, all citizens of the United States of America, trading as RYSTAN COMPANY, of 7, North MacQuesten Parkway, Mount Vernon, New York, United States of America.

THE PATENT OFFICE

D 8152/1(3)/R.109 200 6/64 PL

inflammation, edema (swelling) and pain are prevalent at the site of trauma and many infections in humans. It is an object of this invention to provide novel compositions of matter in the form of tablets useful in controlling inflammation and swelling and as a pain reliever at the site of trauma or infection.

It has been found that the control of inflammation and/or edema or relief of pain due to trauma or infection in humans may be realised by administering to the human an enzyme of the carbohydrase class which is effectively administered by simple application of the carbohydrase enzyme to the buccal mucosa or sublingual mucosa.

More particularly a relatively pure carbohydrase is applied to the buccal area (i.e. between the upper lip and gums) or the sublingual area (beneath the tongue) and maintained in intimate contact with said area for a sufficient period of time to cause the carbohydrase to be effectively applied to the buccal or sublingual mucosa.

Accordingly, the present invention relates to a buccal or sublingual tablet containing a carbohydrase as the active ingredient. The

As indicated hereinabove, the carbohydrase is the principal active ingredient of the tablet of this invention. More particularly, the carbohydrase should be pure and care should be employed to avoid the inclusion of ingredients in significant amounts which tend to cause local irritation in the oral cavity such, for example, as proteolytic enzyes. The carbohydrase used in accordance with this invention, however, need not be completely pure or crystalline. As a practical matter, it is difficult to isolate pure carbohydrases and the presence of other substances which do not inhibit carbohydrase activity or cause local irritation is not a detriment. It is essential, however, that the enzymes used in accordance with this invention be predominantly carbohydrases and that if accompanied by other enzymes, the other enzymes be present in amounts that will not cause local irritation. It is of particular consequence that the proteolytic activity exerted by the tablets of this

[*Price* 4*s.* 6*d.*]

941,664

PATENT SPECIFICATION

NO DRAWINGS

941,664

Date of Application and filing Complete Specification Feb. 19, 1960.

No. 5921/60.

Application made in United States of America (No. 794353) on Feb. 19, 1959.

Complete Specification Published Nov. 13, 1963.

© Crown Copyright 1963.

Index at acceptance: —A5 B2Z.

International Classification: —A61k

COMPLETE SPECIFICATION

Buccal or Sublingual Tablet containing Carbohydrase Enzyme for Controlling Inflammation

We, HENRY THOMPSON STANTON, Jr., JAMES HARRISON STANTON, CHARLES COLLIER STANTON and O'NEILL RYAN, Jr., all Citizens of the United States of America, trading as the firm RYSTAN COMPANY, of 7, North MacQuesten Parkway, Mount Vernon, New York, United States of America, (Assignee of ROBERT DANE BARNARD and HENRY THOMPSON STANTON Jr.) do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to novel compositions of matter in the form of tablets useful in the control of inflammation and/or edema associated with trauma, infection or the like, in humans.

As it well known to those in the field, inflammation, edema (swelling) and pain are prevalent at the site of trauma and many infections in humans. It is an object of this invention to provide novel compositions of matter in the form of tablets useful in controlling inflammation and swelling and as a pain reliever at the site of trauma or infection.

It has been found that the control of inflammation and/or edema or relief of pain due to trauma or infection in humans may be realised by administering to the human an enzyme of the carbohydrase class which is effectively administered by simple application of the carbohydrase enzyme to the buccal mucosa or sublingual mucosa.

More particularly a relatively pure carbohydrase is applied to the buccal area (i.e. between the upper lip and gums) or the sublingual area (beneath the tongue) and maintained in intimate contact with said area for a sufficient period of time to cause the carbohydrase to be effectively applied to the buccal or sublingual mucosa.

Accordingly, the present invention relates to a buccal or sublingual tablet containing a carbohydrase as the active ingredient. The carbohydrase active ingredient acts upon or through the buccal or sublingual membrane to provide anti-inflammatory activity. Excellent results have been obtained from the use of buccal or sublingual tablets containing a carbohydrase in an amount in the range of about 1 to 50 mg., and preferably 2.5 to 15 mg. Typical tablets of this invention are those containing, in an amount of 1 to 50 mg., α amylase of relatively high potency, such as α amylase when incorporated in saline being capable of digesting 150 times its own weight of starch to the achromic point in 10 minutes at a pH of 5.6 and a temperature of 38°C.

As indicated hereinabove, the carbohydrase is the principal active ingredient of the tablet of this invention. More particularly, the carbohydrase should be pure and care should be employed to avoid the inclusion of ingredients in significant amounts which tend to cause local irritation in the oral cavity such, for example, as proteolytic enzyes. The carbohydrase used in accordance with this invention, however, need not be completely pure or crystalline. As a practical matter, it is difficult to isolate pure carbohydrases and the presence of other substances which do not inhibit carbohydrase activity or cause local irritation is not a detriment. It is essential, however, that the enzymes used in accordance with this invention be predominantly carbohydrases and that if accompanied by other enzymes, the other enzymes be present in amounts that will not cause local irritation. It is of particular consequence that the proteolytic activity exerted by the tablets of this

[*Price* 4*s.* 6*d.*]

invention be small when compared to the carbohydrase activity exerted since as indicated above, proteolytic enzymes tend to cause local irritation in the mouth.

The discovery that a carbohydrase when administered buccally or sublingually is an effective anti-inflammatory agent is quite unexpected. Very few drugs can be effectively administered through the buccal mucosa or sublingual mucosa. Secondly, prior to this invention carbohydrases have been administered internally via the oral route, in much greater dosages than those employed in this invention, but this route of administration does not provide the anti-inflammatory effects obtained when the same carbohydrases are administered buccally or sublingually.

The preferred carbohydrase for the tablet of the invention is α amylase. Examples of other carbohydrases which may be applied in accordance with the novel method of this invention are β amylase, glucuronidase, fructosidase, saccharase, dextranase, diastase, arabanase, cellulase, lichenase, chitinase, glycogenase, hyaluronidase, mucinase, inulase, lysozyme, heparinase, xylanase, pectinase, protopectinase, polygalacturonase, pectinase, and pectin depolymerase.

The following are examples of tablets containing a carbohydrase as the active ingredient. In addition to the active ingredients, the tablets contain fillers and binders of such nature that the active ingredient may be applied buccally or sublingually. Of course, the time required for complete administration of the buccal or sublingual tablets of this invention varies depending upon the size of the tablet, its disintegration rate, etc. Preferably, the tablets should be of such size and nature that they may be applied buccally or sublingually within 1/8 to 1 hour.

EXAMPLE 1

Ingredient	Parts (mg.)
α amylase	10
mannitol	66
sodium carboxymethyl cellulose	4

EXAMPLE 2

β amylase	15
β lactose	104

EXAMPLE 3

Hyaluronidase	12.5
dextrose	225.0
sodium carboxymethyl cellulose	12.5

EXAMPLE 4

maltase	15
α lactose	80
sodium carboxymethyl cellulose	5

EXAMPLE 5

lysozyme	5
dextrose	185
sodium carboxymethyl cellulose	10

EXAMPLE 6

polygalacturonase	10
mannitol	66
sodium carboxymethyl cellulose	4

EXAMPLE 7

diastase	50
dextrose	140
sodium carboxymethyl cellulose	10

It has been observed clinically in a number of cases involving humans that inflammation and edema associated with trauma and infection can be controlled by applying buccally or sublingually a tablet containing a carbohydrase as the principal active ingredient. In such cases, there was also observed relief of pain and no irritation of the oral cavity.

WHAT WE CLAIM IS:—

1. A buccal or sublingual tablet for use in controlling inflammation and/or edema associated with trauma, infection and the like in humans, comprising as the active ingredient a carbohydrase in an amount of from 1 to 50 mg., the remaining components of said tablet being of such nature that said carbohydrase may be effectively administered buccally or sublingually without causing local irritation to the oral cavity, the tablet being free from any substantial proteolytic activity and substances causing it.

2. A tablet as claimed in claim 1 in which the carbohydrase is present in an amount of from 2.5 to 15 mg.

3. A tablet as claimed in either of claims 1 or 2 in which the carbohydrase is α amylase.

4. A tablet substantially as hereinbefore described with reference to any one of the Examples.

W. P. THOMPSON & CO.,
12, Church Street, Liverpool, 1.
Chartered Patent Agents.

Leamington Spa: Printed for Her Majesty's Stationery Office by the Courier Press.—1963.
Published at The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.